

CONCEPT

DETAILED PARAMETERS

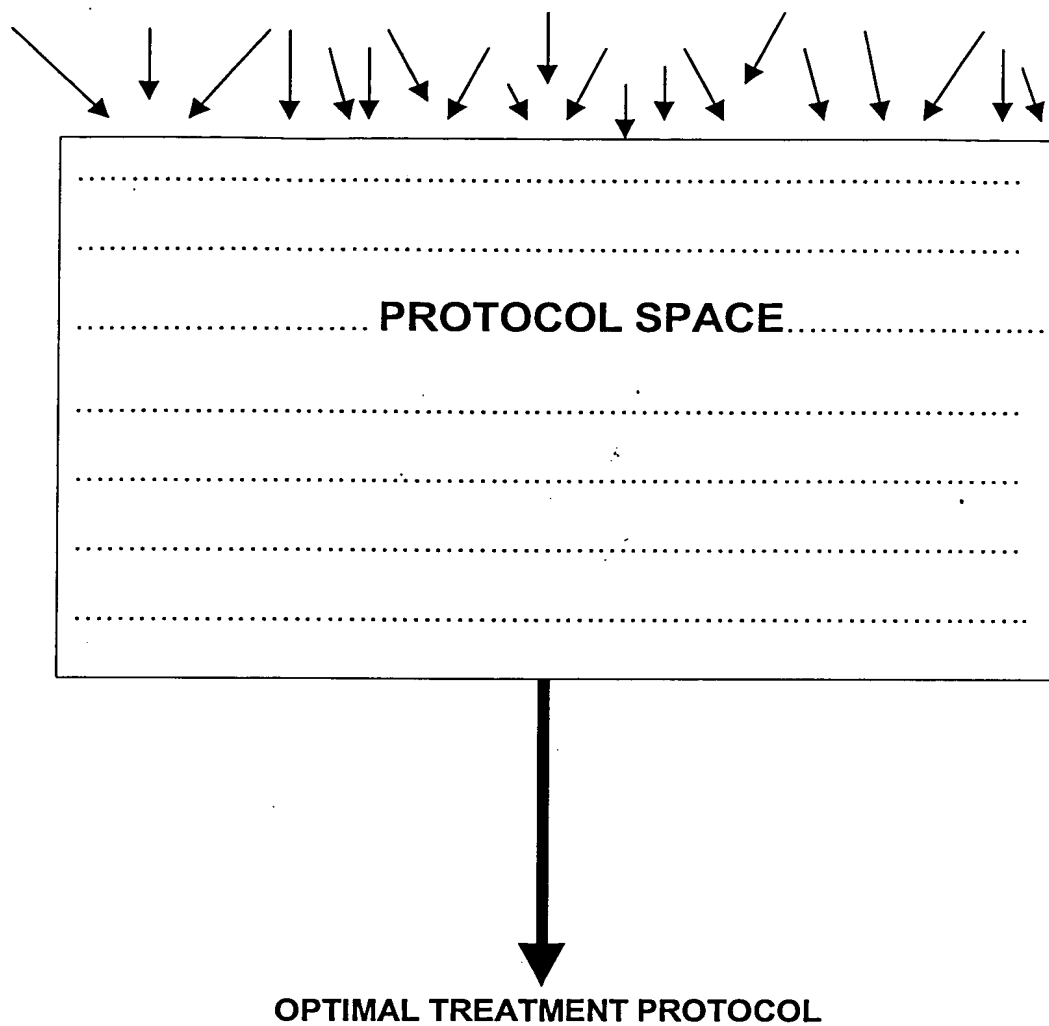


Fig. 1

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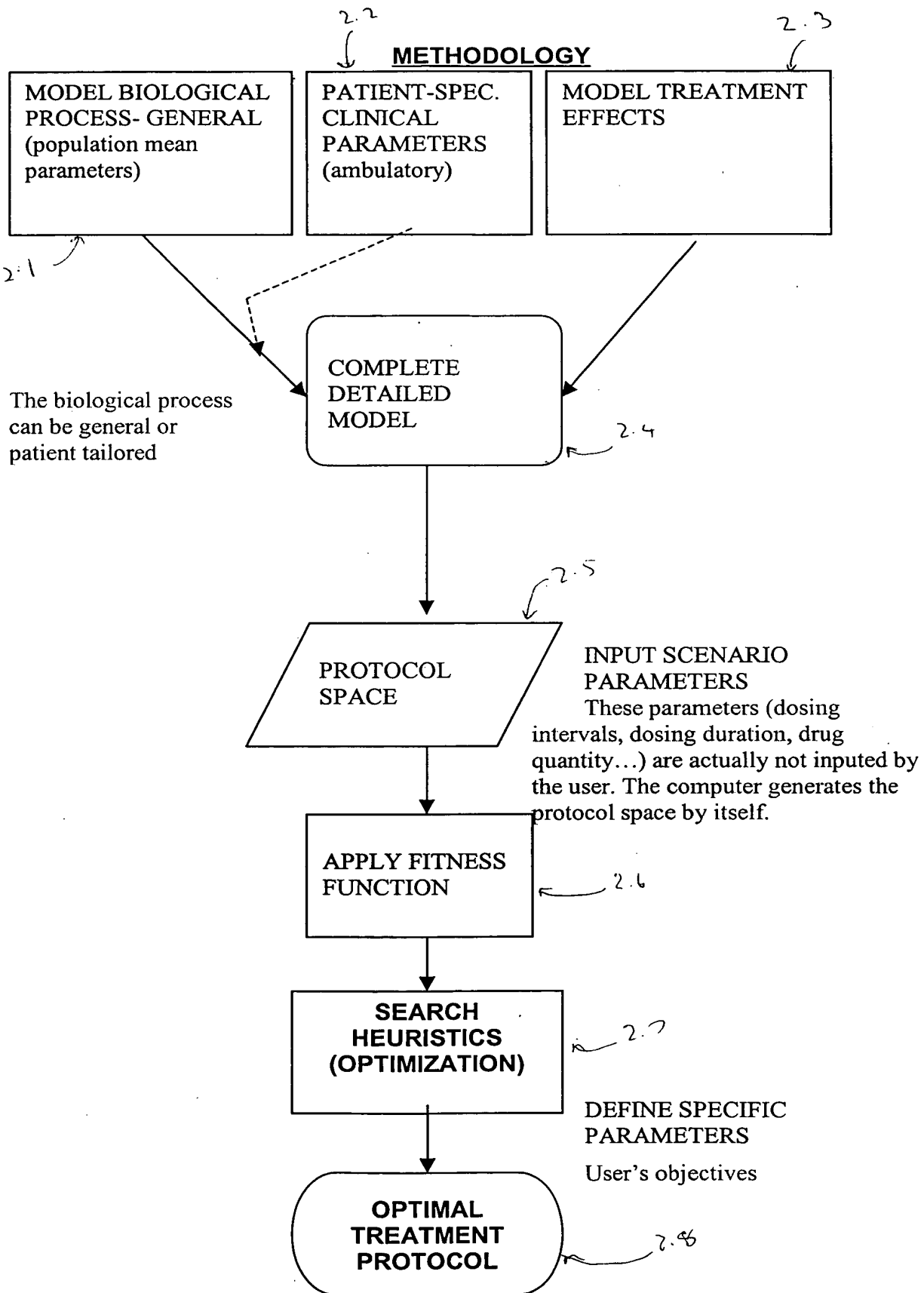


Fig. 2

METHODOLOGY (2)

Attempting to optimize some instance of
a chemotherapy problem with a given
set of solutions...

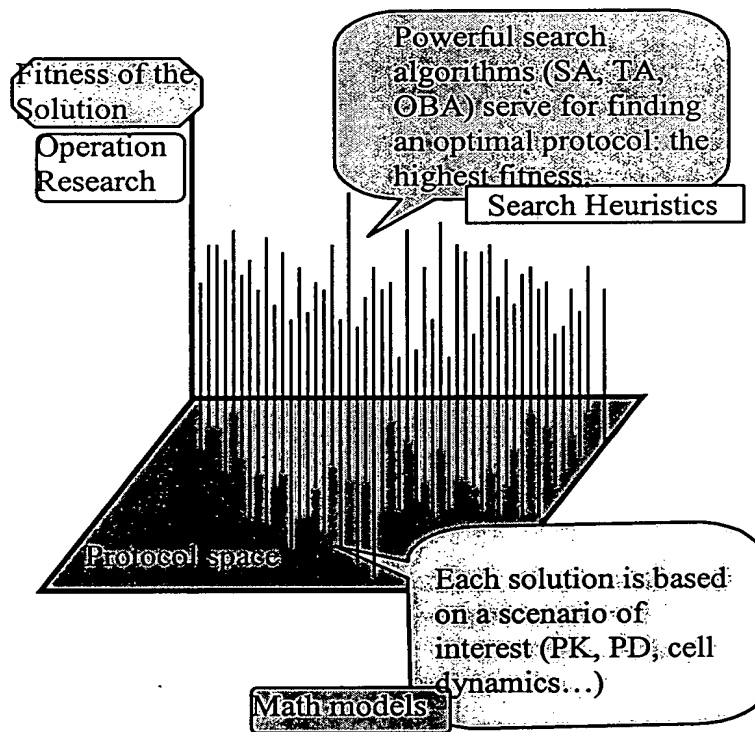
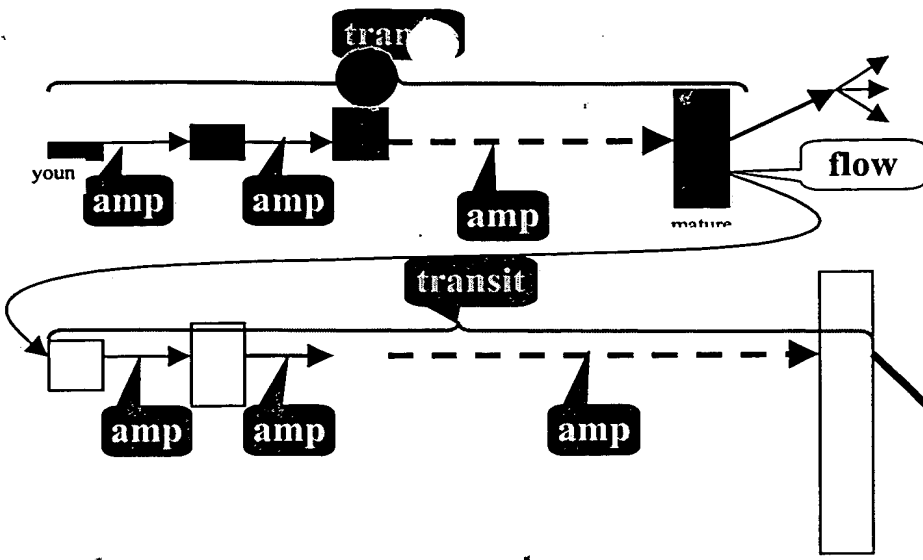


Fig. 2a

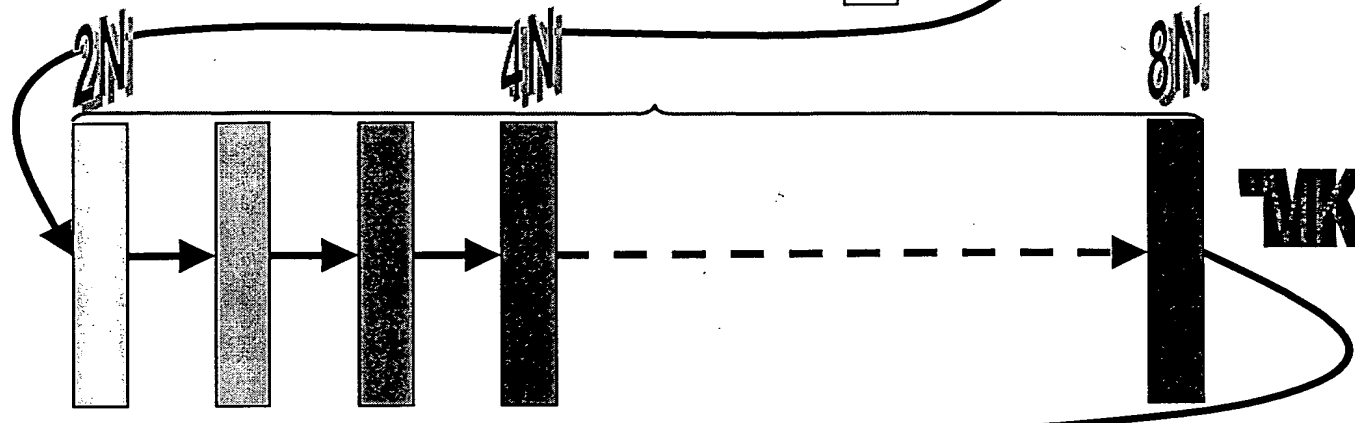
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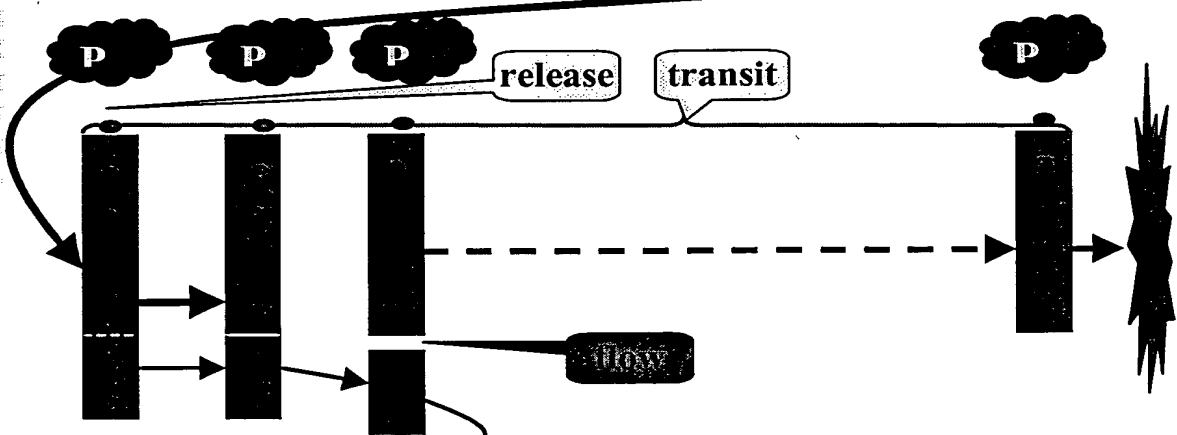


"Stem Cells"

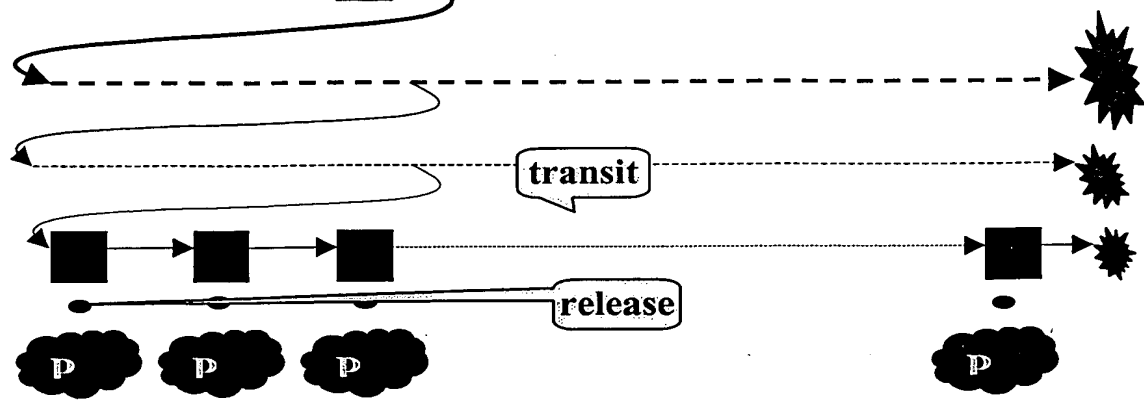
CFU-Meg



"MK3"



MK16



MK32

MK64

MK128

Fig. 3

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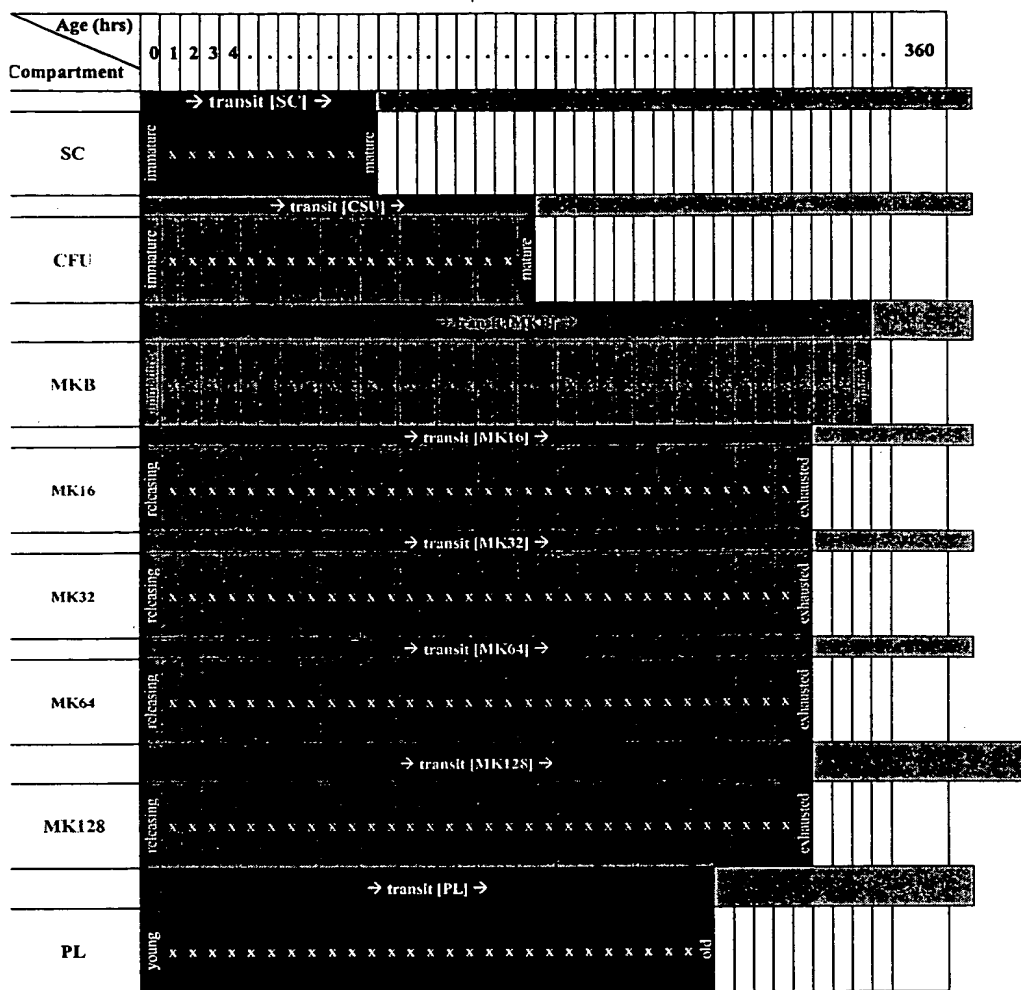


Fig 4

The diagram illustrates the relationship between cell number and cell age in compartments for SC and PL transit times. The y-axis represents 'Cell number' and the x-axis represents 'Cell age in the compartments (hr)'. The diagram shows a step-like increase in cell number over time, with labels for 'SC transit time', 'PL transit time', 'flowing on fraction', and 'endomitosis time'.

Fig. 5

[illegible]

[illegible]

Fig. 6

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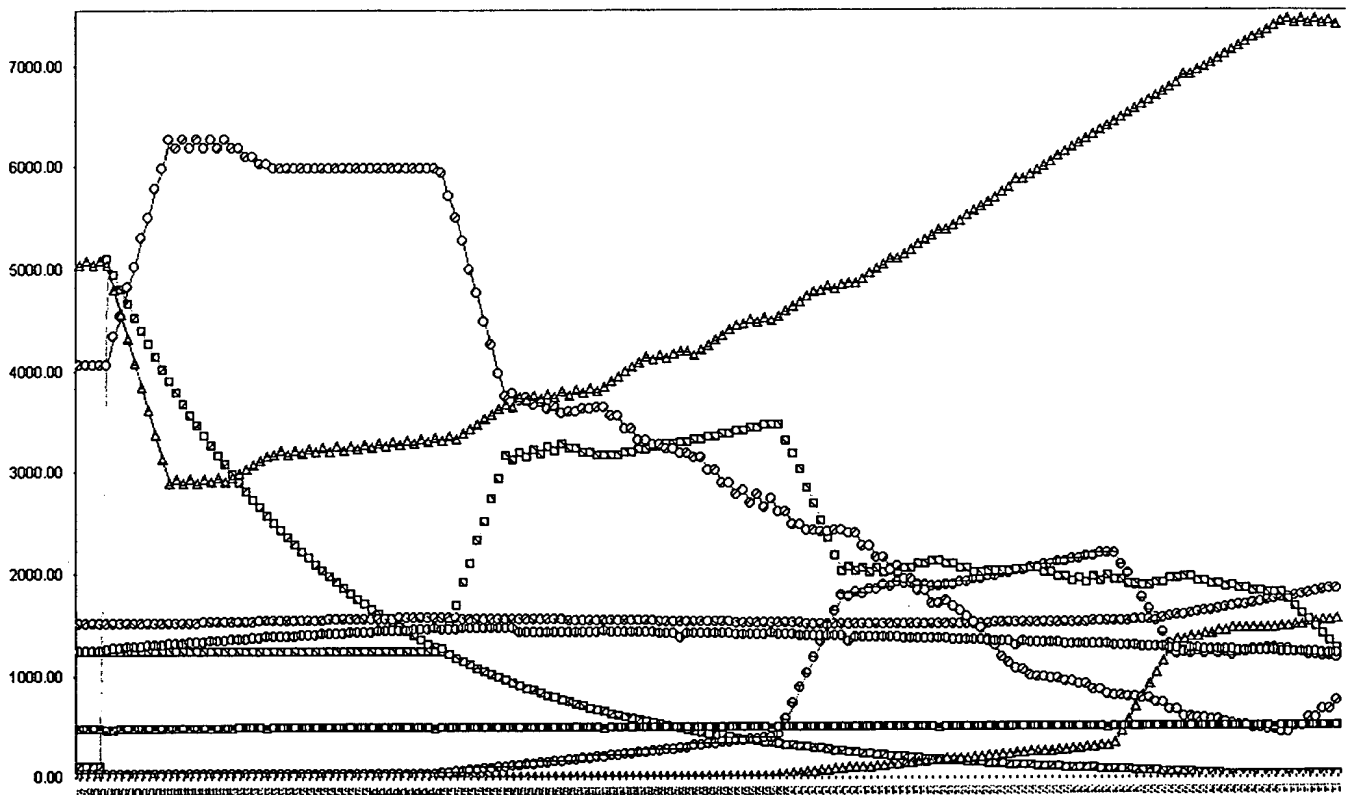


Fig. 7

Simulations showing that if the protocol is pre-calculated then a similar or a higher efficacy can be obtained using 4-fold reduced total dose of TPO.

TPO use in healthy donors:

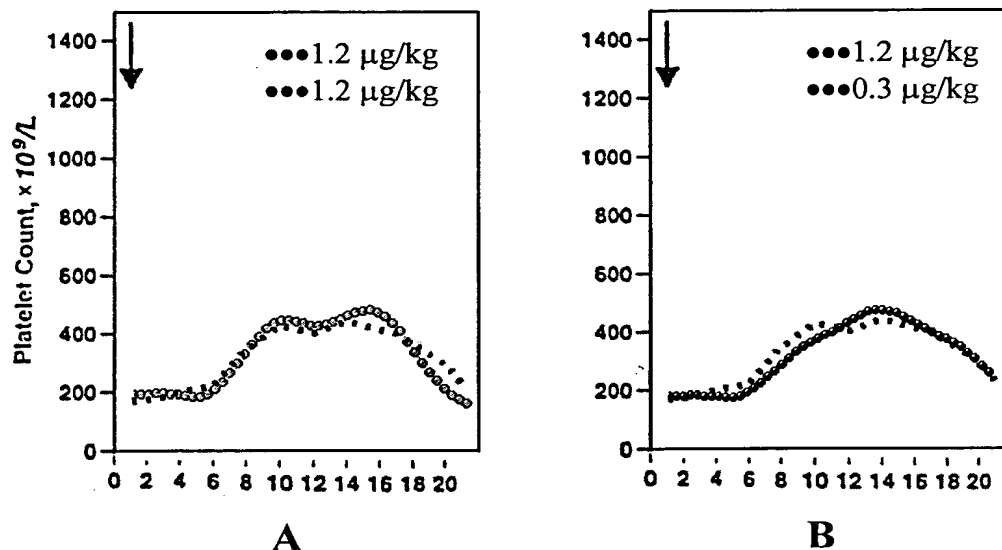


Fig. 8: TPO given to healthy donors- Results of TPO clinical trials from recent research on healthy platelet donors, as compared to our computer simulation results. Arrows indicate the start of TPO treatment. (A) Comparison of experimental data from published articles¹ (black) and our model simulation (green), in both TPO was given as a single IV dose of 1.2 µg/kg on day 0. (B) Comparison of the same experimental data (black) and our proposed TPO administration protocol; the total dose in the simulated protocol was 0.3 µg/kg (blue).

TPO use in patients receiving chemotherapy:

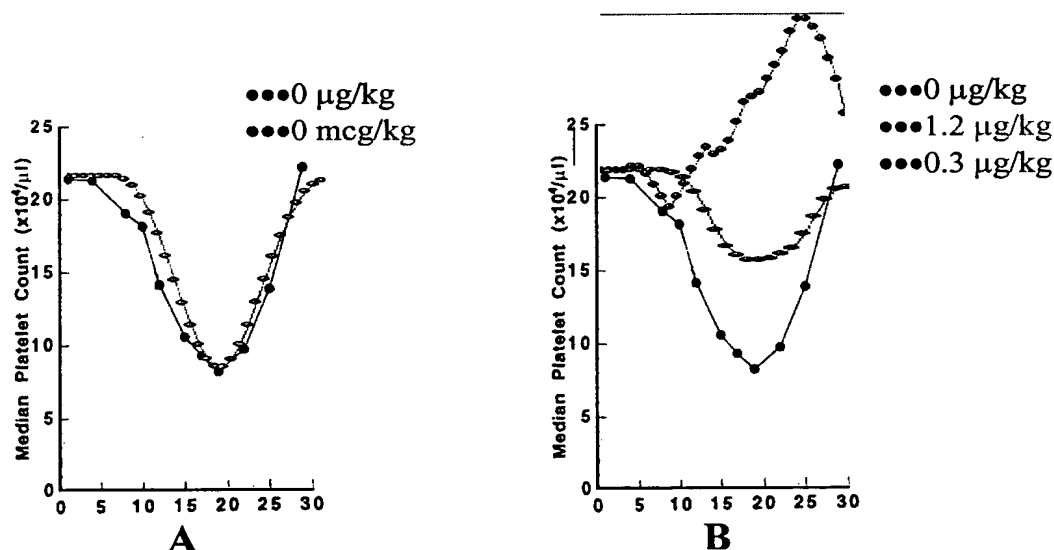


Fig. 9: TPO with chemotherapy- (A) Results of clinical trials from recent research on thrombocytopenia induced in patients receiving single carboplatin chemotherapy² on day 0 (black), as compared to our model simulation of these results (green). (B) The same experimental data (black); simulations of the same experiment, with addition of "conventional" TPO protocol of a single IV dose of 1.2 µg/kg on day 0 (olive); simulations of the same experiment under our proposed protocol that totals 0.3 µg/kg (blue).

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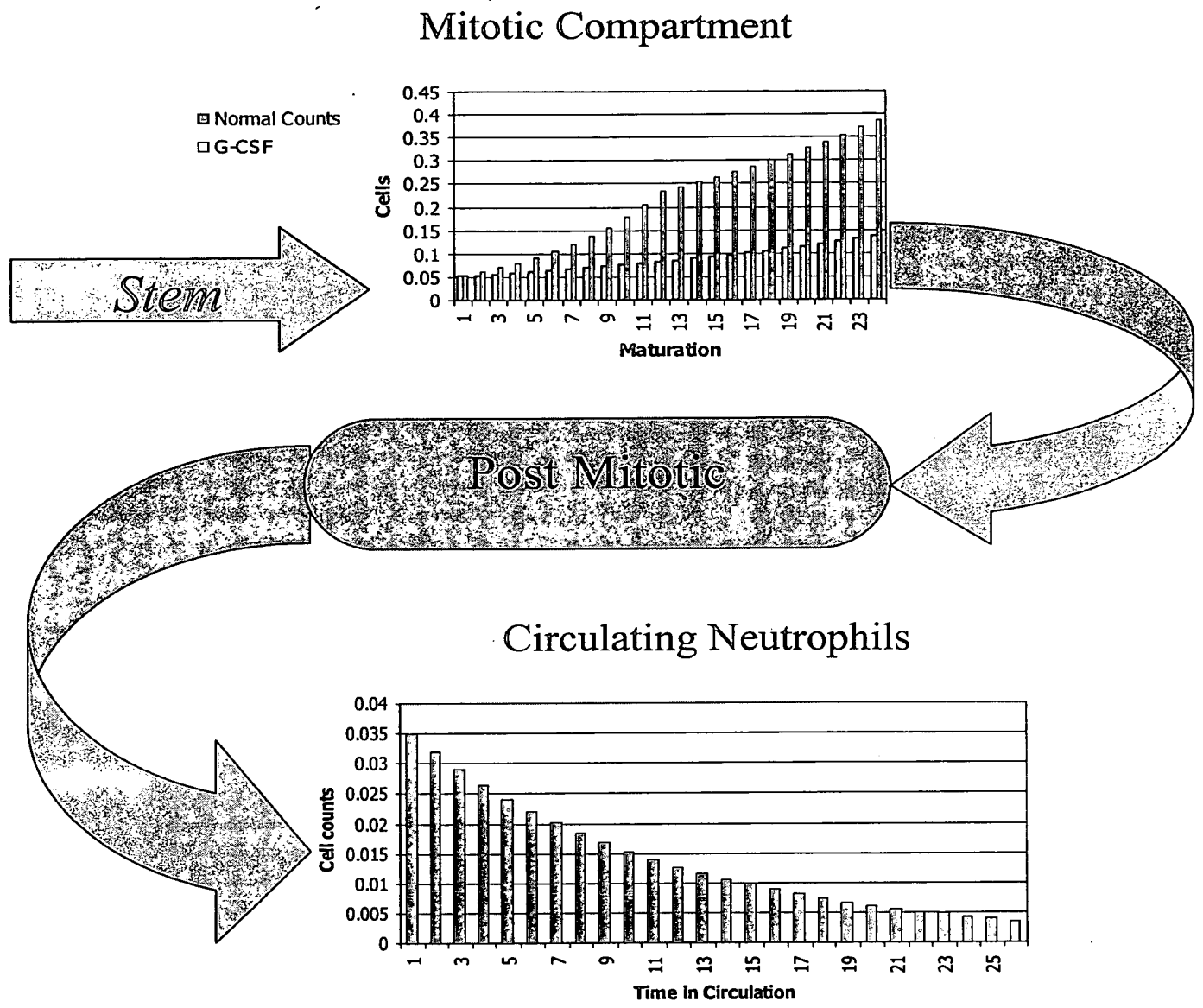


Fig. 10

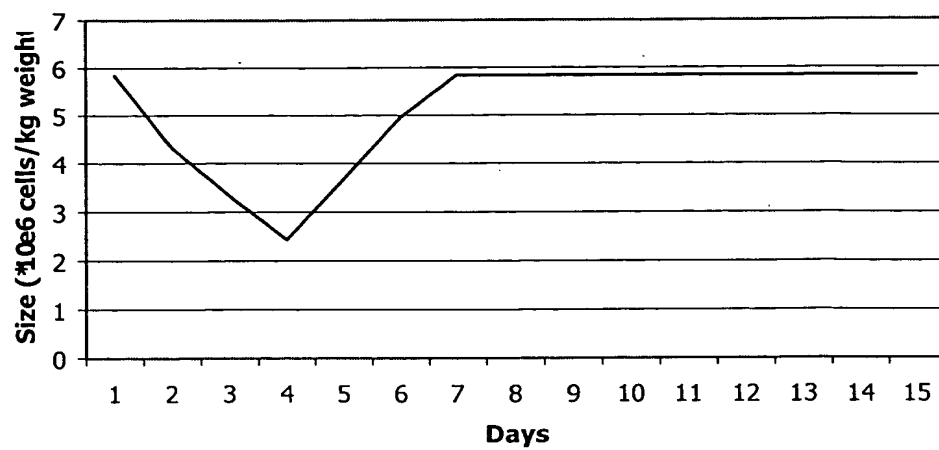


Fig. 11

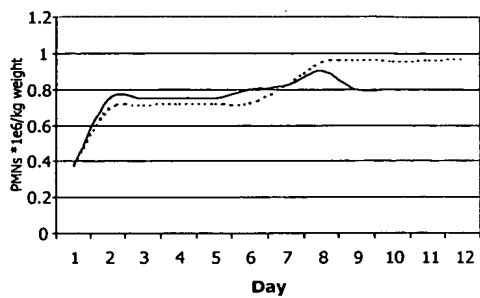


Fig. 12a

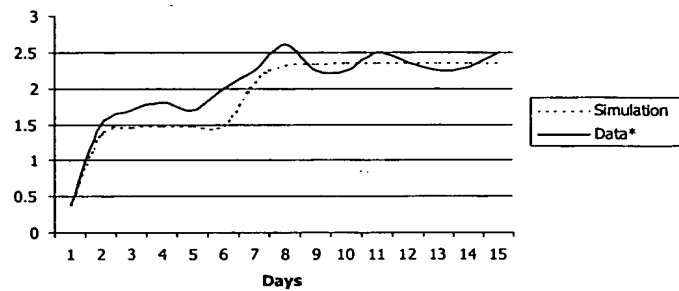
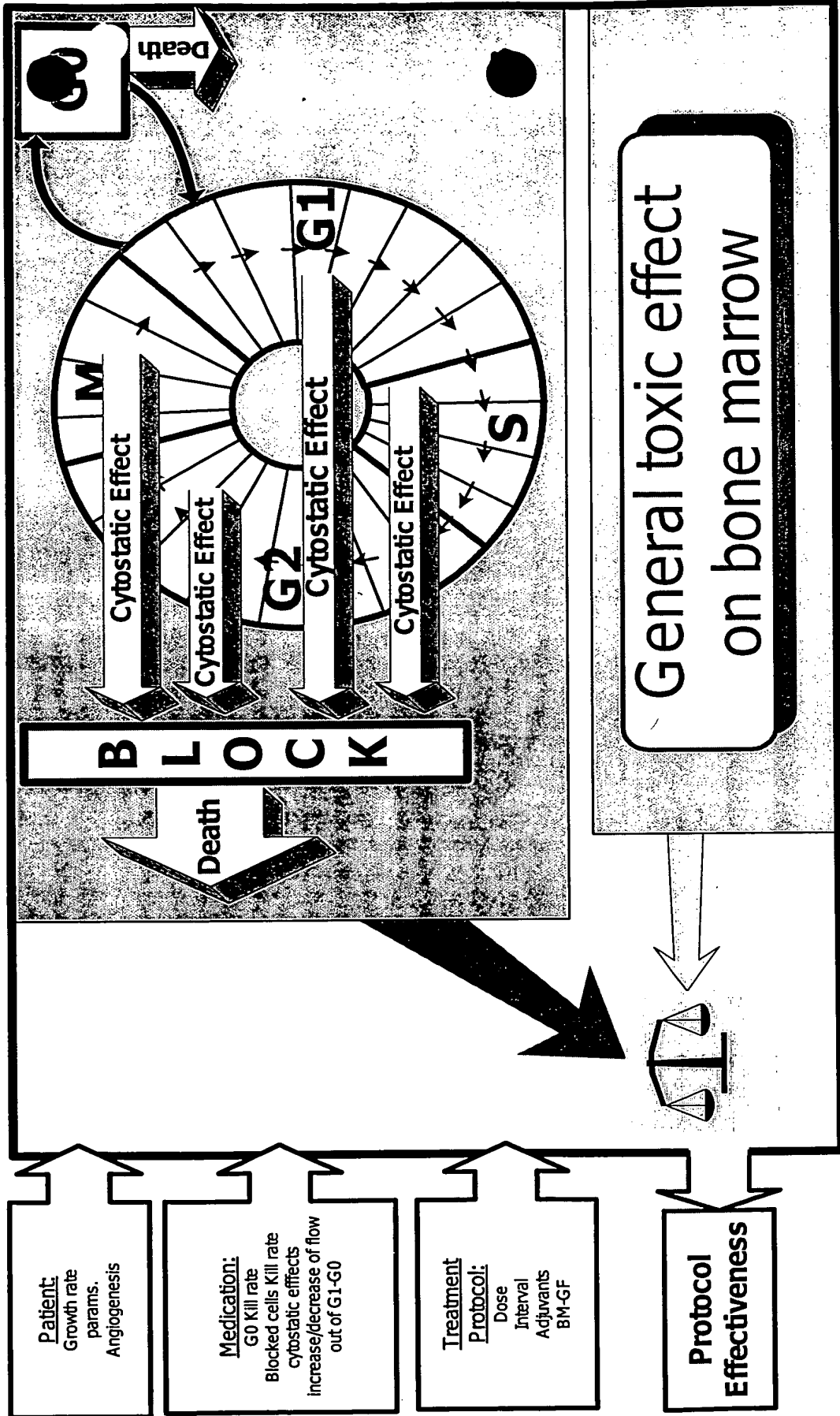


Fig. 12b

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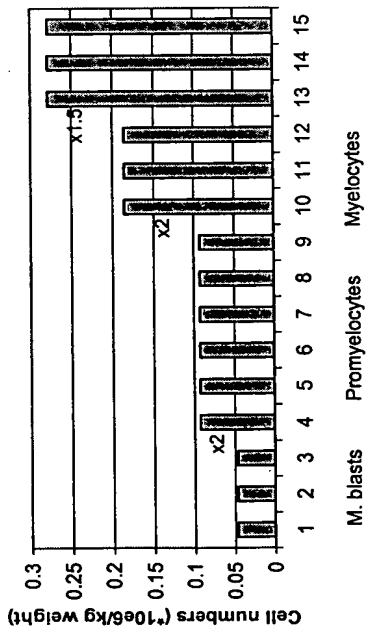


Fig 14. Simulated mitotic compartment age distribution and amplification values in untreated humans. Each bar represents a grouping of 8 cohorts of one hour. Amplification is noted at the place of occurrence.

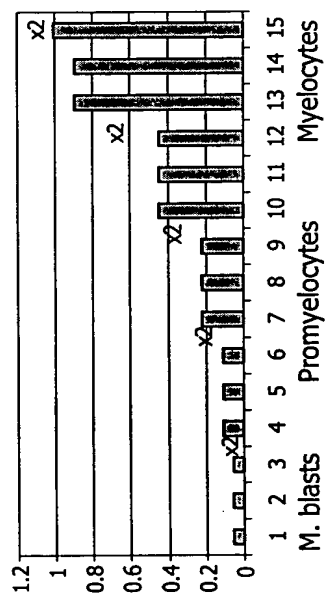


Fig 15. Simulated mitotic compartment age distribution and amplification values in humans treated with 300µg of G-CSF after 15 days. Each bar represents a grouping of 8 cohorts of one hour. Amplification is noted at the place of occurrence. Note, that the last hourly cohort of the Metamyelocytes undergoes mitosis, but its effects are dampened in this graph due to the 8h grouping.